DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/7/09 has been entered.

Previous Claims and Objections/Rejections Status

2. Claims 1,17,19,23,27-36 are pending in the application. Claims 1,17,19 and 23 are directed to an allowable product.

3. The objection to claim 29 is withdrawn.

4. The objection to claims 30-36 is withdrawn.

5. The rejection of claims 27-32 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for physiological, renal, cardiac function monitoring or determining organ perfusion in vivo, does not reasonably provide enablement for all diagnostic procedures is maintained.

6. The rejection of claims 27-36 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn.

7. The rejection of claims 30-32 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps is withdrawn.

Response to Arguments

8. Applicant's arguments filed 10/7/09 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 27-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for physiological, renal, cardiac function monitoring or determining organ perfusion in vivo, does not reasonably provide enablement for all diagnostic procedures. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

1. The nature of the invention, state of the prior art, relative skill of those in the art, and the predictability of the art

The claimed invention relates to a diagnostic procedure, which encompasses any diagnostic procedure. Different diagnostic procedures/techniques require different active agents (i.e. contrast agents) for image enhancement. For example, MRI requires specific nuclei (i.e. gadolinium), CT may use iodinated contrast agents, PET may use ^{18}F, etc. The types of contrast (active) agents required for the different diagnostic techniques/procedures known in the art are well known and predictable to one ordinarily skilled in the art.

2. The breadth of the claims

The claims are very broad and inclusive of "diagnostic procedure" generally, which includes any diagnostic procedure. Also, the claims are so broad that they do not include a specific diagnostic procedure. Clearly, the methods are only used to monitor physiological, renal, cardiac function monitoring and determining organ perfusion via fluorescence or absorbance of the dyes of the instant claims.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction for ascertaining, *a priori*, which diagnostic procedure, except those in which monitor physiological, renal, cardiac function monitoring and determining organ perfusion ***via fluorescence or absorbance*** of the dyes of the instant claims.

4. The quantity of experimentation necessary

There is a lack of adequate guidance from the specification or prior art as to how the instant compounds/dyes would be capable of performing all diagnostic procedures, such as MRI, PET, etc. Applicants fail to provide the guidance and information required to ascertain which diagnostic procedure would be capable of utilizing the instant compounds/dyes without resorting to undue experimentation.

11. Applicant asserts that they disclose how to dose, administer and detect the compounds of the method of the instant claims. Specifically, detection of tracers is achieved by optical fluorescence, absorbance or light scattering methods known in the art using non-invasive probes such as endoscopes, catheters, ear clips, hand bands, surface coils, finger probes and the like (Muller et al.).

12. First, the Muller et al. reference is not listed in an IDS and was not provided for review and therefore is not of record.

13. There is a lack of adequate guidance from the specification or prior art as to how the instant compounds/dyes would be capable of performing all diagnostic procedures, such as MRI, PET, etc which use different forms of detection not related to fluorescence.

New Grounds of Objection/Rejection Necessitated by the Amendment

Claim Objections

14. Claim 29 is objected to because of the following informalities: The instant claim recites, "Y_1 is" and does not provide a substituent(s) for the limitation Y_1. Appropriate correction is required.

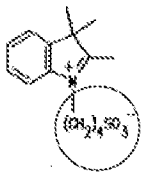
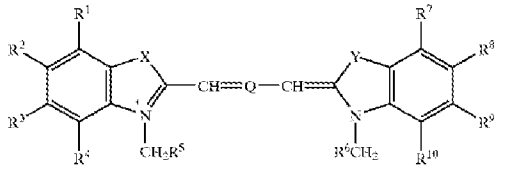
Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 27,29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Licha et al. (US 6,534,041B1) in view of Andrean et al. (US 6,635,090B1).

17. Licha et al. (US 6,534,041B1) discloses the use of cyanine dyes of the disclosure for in-vivo diagnosis of diseased tissue areas with use of NIR radiation, which encompasses the wavelength of light of the instant claims, and for treatment of diseased tissue areas via administration of the cyanine dyes and near infrared radiation (column 7, lines 1-17; claims 10 and 13). The cyanine dye intermediate (I) and the cyanine dye (II) are taught (figure 1). Cyanine dye (II) comprise R^{1-4} and R^{7-10} may be E^1, SO_3E^1, OE^1 where E^1 may be H; X may be O,S, $-C(CH_2R^{13})(CH_2R^{14})$ where R^{13} and R^{14} may be H; R^5 and R^6 may be E^1 where E^1 may be branched or straight-chain C_{1-50} alkyl chain (column 3, lines 19+).

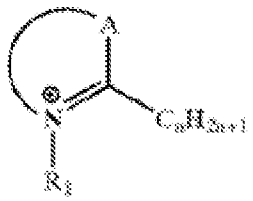
18.  (I)  (II)

19. Licha et al. does not disclose that the substituent circled in red (above)of the cyanine dye (I) encompasses the substituents for the limitation of Y_1 of the instant claims.

20. The cyanine dye (II) comprises R^5 and R^6 which may be branched or straight-chain C_{1-50} alkyl chain which encompasses the C1-C10alkyl limitation for Y_1 of the instant claims. Therefore, at the time of the invention it would have been obvious to one ordinarily skilled in the art that in order to generate the cyanine dye (II), the intermediate (I) must be substituted with the same R^5 and R^6 substituents, such as C1-C10alkyl.

21. Licha et al. does not disclose that the cyanine dye intermediate (I) is used for the method of in-vivo diagnosis.

22. Andrean et al. (US 6,635,090B1) discloses compositions (below), such as 1-butyl-2,3,3-trimethyl-3H-indolium iodide which are dyes used to dye at lease one keratin fiber (abstract; column 1, lines 1-42; claims 22,33). The compound below may comprise R_1 = alkyl groups; A and the nitrogen atom, N, together form at least one hydrocarbon-based ring chosen from unsaturated rings comprising 5 atoms and being fused with at least one ring chosen from unsubstituted or substituted aromatic rings; A is carbon; n = 1 to 4.



23.

24. At the time of the invention it would have been obvious to one ordinarily skilled in the art to utilize the cyanine dye intermediates of Licha et al. for the method of in-vivo diagnosis as Andrean et al. teaches that compounds, such as 1-butyl-2,3,3-trimethyl-3H-indolium iodide having an analogous core ring structure may be used for such a utility, such as dyes. It is noted that keratin fibers are found in epithelium (i.e. squamous cell carcinoma, basal cell carcinoma) and therefore it would have been obvious to one skilled in the art to utilize the cyanine dye intermediates of Licha et al. for the method of in-vivo diagnosis of diseased tissue areas since the dyes having analogous core structures of Andrean et al. are taught for dying keratin fibers (i.e. squamous cell carcinoma).

Conclusion

Claims 1,17,19 and 23 are free of the prior art. As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a). The instant claims 33-36 are objected to for depending on a rejected base claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618